The Diagnosis and Treatment of Adult Urinary Tract Infections in the Emergency Department

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KEYWORDS

• Antimicrobial stewardship • Asymptomatic bacteriuria • Cystitis • Diagnosis
• Diagnostic stewardship • Urinary tract infection

KEY POINTS

- Urinary tract infection (UTI) diagnosis should be made in the presence of genitourinary symptoms and signs combined with findings from urinalysis and/or urine culture. Laboratory findings alone cannot diagnose UTI.
- Empirical selection of antimicrobials for UTI should consider patient-specific risk factors for resistance as well as local community resistance patterns as determined by emergency department (ED)-specific urinary antibiograms.
- There are numerous antimicrobial stewardship interventions that can improve diagnosis and management of UTIs in the ED.
- Consideration should be given to the possibility of sexually transmitted infections and less common but potentially serious conditions such as ureterolithiasis with infection.

INTRODUCTION

Emergency medicine has been called the art of "making complicated clinical decisions with limited information." This description is particularly relevant in the case of diagnosing and treating urinary tract infections (UTIs) in the emergency department (ED).[1] Appropriate diagnosis and management of UTIs in the ED can feel like stitching together a series of probabilities, where the accuracy of the clinical decisions can only be known days later, if ever.

Are these urinary symptoms? Are these urinalysis (UA) findings caused by pathologic bacteria, colonizing bacteria, or a contaminated specimen? If pathologic, what are the offending bacterial organism and what antibiotics might have activity against

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this organism? Will the patient tolerate the effective antibiotics or have an adverse reaction? What if I am asked to "cold call" a patient whom I have not seen? Few areas of medicine blur art and science like UTIs in the ED.

The recommendations provided here represent a multidisciplinary (infectious diseases pharmacist, emergency medicine physician) interpretation of the primary literature and current practice guidelines. Our objective is to add as much clarity as possible to an inherently unclear process of UTI diagnosis and offer a practical approach to the treatment of UTIs in the ED. We pay special attention to ED-specific conundrums, such as the approach to the elderly patient with an indwelling catheter and antibiotic stewardship considerations tailored to the ED. Whether you read this article in its entirety, to become the UTI guru of your ED, or skip to the section that is relevant to the patient in front of you, we offer guidance that is practical, evidence-based, and laser-focused on the real-world ED experience.

EPIDEMIOLOGY

Over 1 million ED visits for UTI occur annually in the United States.[2] The majority of UTIs are cases of uncomplicated cystitis occurring in women.[3,4] The exact incidence of uncomplicated cystitis varies by patient population, with a reported rate of approximately 0.7 cases per person year in young women.[5] It is commonly accepted that the lifetime risk of having at least one UTI is upward of 50% in women of reproductive age.[6] In addition, regardless of sex, the risk of developing UTI increases with age. The lifetime prevalence of UTI in men is 20%. The incidence of UTIs in men is approximately 0.9 to 2.4 cases per 1000 persons aged less than 55 years but increases to 7.7 cases per 1000 persons once age 85 is reached.[7]

MICROBIOLOGY AND ANTIMICROBIAL RESISTANCE

The most common causative organism remains *Escherichia coli,* causing over 75% of uncomplicated UTIs. Other *Enterobacterales* such as *Klebsiella pneumoniae* and *Proteus mirabilis*, as well as *Staphylococcus saprophyticus* are also common causes of uncomplicated UTI. Complicated UTIs represent a smaller fraction of ED visits but more often result in admission to observation units or hospitalization.[4,8] Among patients with complicated UTI presenting to the ED (**Tables 1** and **2**), *Enterobacterales* species remain the primary cause of infection with *E coli* being the dominant pathogen,[9] but there is more diversity in the potential causative organisms and associated resistance patterns, including isolation of both *Pseudomonas* and *Staphylococcus aureus.*

Antibiotic resistance in the outpatient setting is on the rise, which is particularly true with respect to urinary pathogens. Variables that have been associated with increased risk of antibiotic resistance include advanced age, use of fluoroquinolones, and residence in a skilled nursing facility.[10,11] When examining recent data for *E coli* urinary isolates, resistance to commonly prescribed agents such as trimethoprim/sulfamethoxazole (TMP/SMX) often approached or exceeded 20% for cystitis and 10% for pyelonephritis—the thresholds at which empirical use of that agent should be abandoned.[12,13] In a multicenter 2019 study of ED patients with UTI caused by *E coli*, 25% were resistant to TMP/SMX.[14] Resistance of urinary isolates to fluoroquinolones is also steeply on the rise. In a 2018 to 2020 study conducted in 15 geographically diverse EDs across the United States, fluoroquinolone resistance was found in 22% of *E coli* isolates overall and exceeding 25% in several EDs.[15] Furthermore, most patients had no identifiable risk factor for resistance. Fortunately, rates of resistance to nitrofurantoin among uropathogens generally remain less than 10%.[12] The prescription of nitrofurantoin is associated with a decreased risk inadequate empirical

Table 1
Categorizations and definitions of urinary tract infection: categorizations of urinary tract infection

UTI Category	Patient Characteristics	Presentation	Cautions	Diagnostics	Treatment Issues
ASB	Bacteriuria, with abnormal UA or positive urine culture, absent urinary signs, symptoms, or fever. In the majority of patients, ASB is not a pathologic infectioous state. It should not be treated and should not prompt a urine culture.				
Uncomplicated cystitis	Young healthy women, nonpregnant	Dysuria, increased urinary frequency, and suprapubic tenderness	Always consider STI[a]	Consider urine culture, especially for history of recent treated UTI; consider STI testing	Nitrofurantoin is first line. Consider symptomatic treatment with NSAIDs and phenazopyridine
Complicated[b] cystitis	Men, elderly, indwelling catheter	Dysuria, increased urinary frequency, and suprapubic tenderness	Young men with voiding symptoms have an STI (not UTI) until proven otherwise; consider epididymitis and prostatitis	Urine culture advised; if catheter is present, exchange prior to UA/ urine culture	Nitrofurantoin or fosfomycin is first line. Consider resistant pathogens
Prostatitis	Men of any age, especially if known enlarged prostate	Dysuria, increased urinary frequency, incontinence, hesitancy, fever	Consider prostate abscess or STI	Urine culture mandatory; consider CT for abscess and STI testing	Consider admission; Fluoroquinolones are first line for outpatient therapy. Consider resistant pathogens
Uncomplicated pyelonephritis	Young, otherwise healthy women, nonpregnant	Fever, flank pain; dysuria, and frequency may be absent; may present with sepsis	Occult obstruction (eg, ureteral stone) rare, but cannot be missed	Urine culture mandatory; POCUS for hydronephrosis advised	Consider initial parenteral antibiotics if febrile/toxic; outpatient oral treatment usually possible
Complicated pyelonephritis	Men, elderly, comorbidities, recent health care exposure	Fever, flank pain; may present with bacteremia or sepsis	Consider CT for obstruction, perinephric abscess, and so forth	Urine culture mandatory; consider blood cultures	Admission generally required; IV broad spectrum coverage

[a] Sexually transmitted infections (STIs), in the context of urinary symptoms, typically include gonorrhea, chlamydia, syphilis, and trichomonas. *Gardnerella vaginalis* may also present with urinary symptoms and is sometimes classified as an STI.
[b] See definition of Complicated UTI in Table 1B.

Table 2
Categorizations and definitions of urinary tract infection: definition of "complicated" urinary tract infection

"Complicated" refers to host factors that may confer risk for poor response to standard, narrow spectrum therapy

Class of Complication	*Specific Factors*
Urinary tract obstruction	Pregnancy, benign prostatic hyperplasia (older men), neurogenic bladder, urinary catheter, renal stone, ureteral stone, ureteral stricture
Immunosuppression	Diabetes, elderly, transplant, immunosuppressive medications, AIDS
Risk for multi-drug resisitance uropathogens	Previous infection or colonization with an antibiotic resistant pathogen, recent broad-spectrum antibiotics, recent or extensive health care exposure, residence in nursing home or long-term care facility, urinary catheter

therapy for lower tract UTIs.[16] In addition to increasing rates of resistance to guideline-recommended first-line oral antibiotics, resistance to beta-lactam antibiotics, which are often used to treat UTIs requiring hospitalization, is also on the rise. Among urinary isolates collected from outpatients and ED patients hospitalized for UTIs between 2010 and 2020, extended-spectrum beta-lactamase-producing Enterobacterales, such as *E coli* and *Klebsiella*, which are resistant to cephalexin and third-generation cephalosporins like ceftriaxone, were present in 7% to 17% of isolates.[13,17] Extended spectrum beta-lactamase (ESBL)-producing isolates increased 30% from 2011 to 2020. In a recent study of empirical antibiotic choices in the ED that focused on UTIs caused by Enterobacterales, among over 5000 episodes, 22% received discordant therapy, where the urinary pathogen was resistant to the initial antibiotic.[10] Discordant empirical therapy for UTIs is associated with worse downstream outcomes.[18,19] Those that received an initially ineffective agent were twice as likely to be hospitalized within the next 28 days (**Box 1**).

DIAGNOSIS AND TREATMENT OF URINARY TRACT INFECTION IN THE EMERGENCY DEPARTMENT

Focal genitourinary symptoms and signs of a UTI include urinary urgency, frequency and dysuria, and suprapubic and costovertebral angle tenderness.[22] Elderly patients without focal genitourinary symptoms are considered asymptomatic.[23,24] It is important to note that sexually transmitted infections also cause lower UTI symptoms, whereas pyelonephritis frequently presents as fever and costovertebral angle tenderness without lower genitourinary symptoms.

Box 1
Risk factors for antibiotic-resistant uropathogens[14,20,21]

Previous hospitalization in the last 30 days

IV antibiotic use in the last 90 days

Previous UTIs (especially with previously isolated resistant pathogen)

Chronic renal dialysis

Previous history of urologic procedure or urinary tract abnormality

Residence in nursing home or rehabilitation facility

Major categories of UTI are uncomplicated cystitis, complicated cystitis, prostatitis, uncomplicated pyelonephritis, complicated pyelonephritis, and severe UTI that presents as sepsis from a suspected urinary source. While asymptomatic bacteriuria (ASB) is not technically a pathologic infection state, it should be considered in the categorization scheme, as ASB is commonly encountered and is a key driver of antibiotic overprescribing. These categorizations are important because empirical antibiotic selection begins with the type of UTI being considered. They are summarized in **Tables 1** and **2** and described in detail.

Uncomplicated cystitis is the most common bacterial infection in women. Uncomplicated cystitis is classically defined as frequency and dysuria without fever occurring in an immunocompetent, nonpregnant woman who has no comorbidities or urologic abnormalities. A woman with dysuria and urinary frequency in combination with the absence of vaginal discharge or vaginal irritation has a 77% posttest probability of having uncomplicated cystitis, regardless of UA results.[25] In such cases, physical examination is often normal or just positive for suprapubic tenderness.[26] Complicated cystitis refers to a UTI that is localized to the bladder but carries a higher risk of treatment failure due to host factors such as male, pregnant, elderly, indwelling catheter, and immunocompromised (see **Tables 1** and **2**). Signs and symptoms are generally similar to uncomplicated cystitis; however, first-line antibiotic treatment recommendations may differ based on the complicating factor.

Acute prostatitis typically occurs when an organism from the urinary tract refluxes into the male prostate via the prostatic ducts.[27] Acute prostatitis can occur in healthy men at any age; however, it is more common in the context of urethral obstruction or recent urologic instrumentation. Prostatitis can present as dysuria as well as urinary retention, incontinence, and hesitancy. Fever may be present. There may be symptoms or signs related to concomitant infection in the bladder or epididymis. The onset of symptoms can be subtle, and the duration of illness may last for weeks.

Uncomplicated pyelonephritis is an upper urinary tract infection without any complicating host factors.[28] Because the infection has ascended into the ureter and kidney, voiding symptoms may be absent entirely. Symptoms and signs include flank pain, chills, nausea, vomiting, with fever and costovertebral tenderness and fever. Lower genitourinary symptoms may also be present. While patients with uncomplicated pyelonephritis may present systemically ill with abnormal vital signs, outpatient therapy is often possible if there is a good response to initial ED therapies. Complicated pyelonephritis presents with similar signs and symptoms; however, patients who are systemically ill are less likely to respond well to initial ED therapy and generally require hospital admission. In essence, complicated pyelonephritis should be investigated and treated with a high degree of suspicion for sepsis, bacteremia, and a resistant uropathogen. Empirical broad-spectrum intravenous agents may be appropriate based on the specific complicating factors.

URINE TESTING

Urine testing in the ED typically includes a UA, with or without urine culture depending on the category of UTI and patient risk factors for multidrug-resistant organisms. Point of care urine dipstick testing is used in some acute settings, such as urgent cares or low-resource EDs. As with all medical testing, ED urine testing is most effective when ordered appropriately (moderate pretest probability of disease), collected appropriately (midstream, clean catch), and interpreted appropriately (a nuanced topic). In fact, a patient with a high probability of uncomplicated cystitis after history and physical alone requires no urine testing at all (**Fig. 1**).

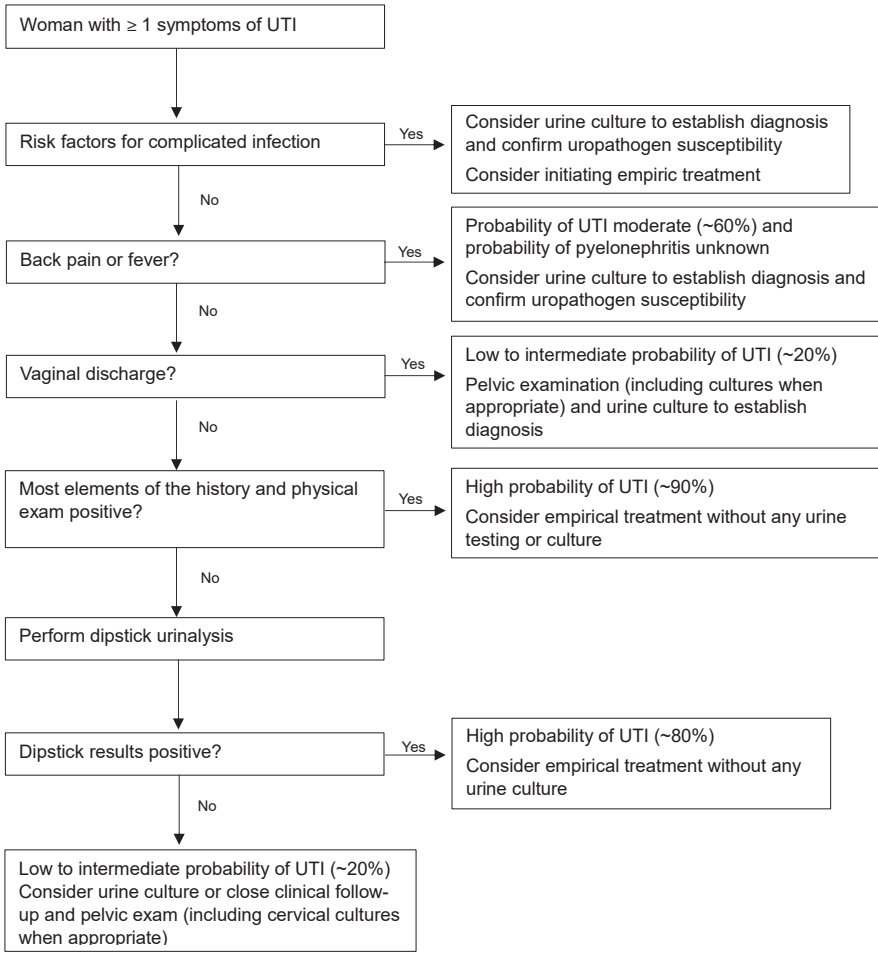
Woman with ≥ 1 symptoms of UTI
Risk factors for complicated infection
Yes
Consider urine culture to establish diagnosis and confirm uropathogen susceptibility
Consider initiating empiric treatment
No
Back pain or fever?
Yes
Probability of UTI moderate (~60%) and probability of pyelonephritis unknown
Consider urine culture to establish diagnosis and confirm uropathogen susceptibility
No
Vaginal discharge?
Yes
Low to intermediate probability of UTI (~20%)
Pelvic examination (including cultures when appropriate) and urine culture to establish diagnosis
No
Most elements of the history and physical exam positive?
Yes
High probability of UTI (~90%)
Consider empirical treatment without any urine testing or culture
No
Perform dipstick urinalysis
Dipstick results positive?
Yes
High probability of UTI (~80%)
Consider empirical treatment without any urine culture
No
Low to intermediate probability of UTI (~20%)
Consider urine culture or close clinical follow-up and pelvic exam (including cervical cultures when appropriate)

Fig. 1. Diagnostic algorithm for suspected uncomplicated cystitis.[25,30]

Dipstick, Microscopic Urinalysis, and Urine Culture

The urine specimen for UTI testing should be collected in such a way that it is as free as possible from skin and vaginal debris and contaminating bacteria, which entails a midstream clean catch or an in-and-out straight catheter sample. A urine culture is generally unnecessary in uncomplicated cystitis but is recommended if there is concern for a complicated UTI, pyelonephritis, resistant organisms, or treatment failure. Indwelling urinary catheters should be exchanged prior to obtaining the urine sample. In the case pyelonephritis or sepsis, a reasonable effort should be made to obtain a urine culture specimen prior to initiating antibiotics.

The urine dipstick is a rapid, inexpensive point of care substitute for the UA. Components tested vary by brand but typically include specific gravity, pH, protein, leukocyte esterase, nitrites, blood, ketones, glucose, bilirubin, and urobilinogen.[31] Dipstick testing does not evaluate for the presence of squamous epithelial cells or bacteria. Common causes of false positive and false negative dipstick results are shown in **Table 3**. A completely normal urine dipstick may have a negative predictive value

Table 3
Selected common pitfalls of urine dipstick testing[32]

Leukocyte Test False Positives	Leukocyte Test False Negatives	Nitrite Test False Positives	Nitrite Test False Negatives
Contamination from vagina or foreskin secretions	Increases in urine-specific gravity or glucose	Prolonged exposure of dipstick to air prior to testing	Many gram + organisms do not produce nitrites
Expired dipstick	Presence of urine ketones or protein	Expired dipstick	Urine that has not been in the bladder more than 4 hours
Improperly stored dipstick	Use of vitamin C or certain antibiotics	Medications causing reddish urine color (eg, Pyridium)	Urine pH <6, high urobilinogen or specific gravity
Discolored urine from food or medications (eg, nitrofurantoin)	Less than room temperature urine sample	Urine sample more than 4 hours old	Patients with low nitrate diet

Adapted from Eriksen, Stine Veronica, and Pia Cecilie Bing-Jonsson. "Can we trust urine dipsticks?." Nor J Clin *Nurs/Sykepl Forsk* 10.1 (2017): 1-14.

for UTI as high as 90% to 95%.[36] However, multiple systematic reviews and meta-analyses demonstrate that dipstick performance is nonspecific, so a "positive urine dipstick" (variably defined) does not reliably confirm the diagnosis of UTI.[37–39] As such, the dipstick analysis remains useful in certain outpatient settings as a first-level screening test (see **Tables 1** and **2**).

A complete UA includes a physical, chemical, and microscopic examination of the sample. Over time, there have been various *en vogue* aspects of the UA, held up as more sensitive or specific for diagnosing or excluding UTI. This has resulted in an inconsistent approach among clinicians, where one regards the presence of leukocyte esterase as the key to the diagnosis, whereas another may hang their hat on the presence of nitrites. Most studies have shown that leukocyte esterase and leukocytes lack specificity (can be falsely positive), whereas nitrites are more specific (fewer false positives), but lack sensitivity (can be false negative). **Table 4** demonstrates the positive likelihood ratios (which incorporate both true and false positive rates) for components of the UA.

A confirmatory urine culture is recommended, if appropriate, for formal diagnosis of a UTI. The quantitative urine culture remains the gold standard method for diagnosis of UTI. Urine cultures require up to 18 hours for bacterial growth on culture media by standard laboratory techniques, so real-time ED diagnosis based on urine culture is not feasible.[40] Cutoffs for the number of colony-forming units (CFUs) that define significant uropathogen growth vary. For example, the US Centers for Disease Control and Prevention require 100,000 CFU/mL to meet the criteria for diagnosis of UTI, while the Infectious Disease Society of America sets a lower threshold of 50,000 CFU/mL when a single, common uropathogen (ie, *E coli*) is isolated.[41] In general, young, well-hydrated women with cystitis may grow fewer colonies on culture.

Many EDs have an automatic reflex order for urine culture if pyuria is present, which runs the risk of triggering a urine culture in the absence of UTI symptoms. The prevalence of pyuria in women with ASB is estimated to be 32% overall and increases to 90% in the elderly.[42,43] This underscores the importance of testing urine only when symptoms are present, as inappropriately sent urine cultures in the elderly often leads to antibiotic treatment of ASB.

Imaging

Cross-sectional imaging is typically not warranted for UTI diagnosis or management decisions, but may be considered for patients who are septic, have suspected obstruction of the urinary tract, and have persistent clinical symptoms despite 72 hours of antimicrobial therapy. Outpatient clinicians, especially urologists, may also image patients who have recurrent infection within a month of treatment. The goal of cross-sectional imaging is to diagnose UTI complications (ie, perinephric abscess) or an anatomic feature that requires surgical intervention (ie, obstructing ureteral stone).[29] Contrast-enhanced CT, often obtained to investigate fever or abdominal

Table 4
Positive likelihood ratios for selected urinalysis and urine culture findings[33–35]

Bacteriuria	4.7
Leukocyte Esterase	4.2
Nitrites	4.2
Pyuria	3.3
>10^2 CFU/mL of *E coli*	6.3

pain of unclear cause, may reveal a wedge-shaped hypoattenuated region of renal parenchyma with perinephric fat stranding, indicating acute pyelonephritis. Some authors have proposed that point of care ultrasound should be performed routinely in all cases of febrile pyelonephritis or urosepsis to rule out hydronephrosis from an obstructing ureteral stone.

Urinary tract infection diagnostic algorithm

One evidence-based yet sensible way to approach the diagnosis of female UTI in the ED is to follow a stepwise algorithm, such as that proposed by Bent and colleagues (see **Fig. 1**). This approach takes into account whether or not there are signs of upper urinary tract involvement or features that would make the UTI complicated, and whether vaginitis or a sexually transmitted infection could account for the symptoms, in order to guide what urine testing is required (if any) and arrive at a likely diagnosis.[25,30]

URINARY TRACT INFECTION THERAPY

In addition to antimicrobial treatment for UTIs, it is important that emergency providers consider simultaneous treatment of associated sepsis and other symptoms and consider whether procedural source control might be required. Patients with cystitis and prominent voiding symptoms and lower abdominal discomfort should be prescribed a nonsteroidal anti-inflammatory drug and phenazopyridine (a bladder analgesic) for 2 days. Young female patients with otherwise uncomplicated pyelonephritis who initially present with fever and systemic toxicity should be treated aggressively with antipyretics, analgesics, IV crystalloids, and a single dose of parenteral antibiotics. Those with evidence of sepsis-related organ dysfunction or lactic acidosis should undergo state-of-the-art sepsis management. However, in many cases, an initially toxic but otherwise healthy young patient will "turn around" within a few hours and prove stable for discharge home to complete a course of oral antibiotic therapy. A small but critical subset of pyelonephritis cases are associated with ureteral obstruction, which can be difficult to discern by history and physical alone (hence, the recommendation abovementioned to consider routine POCUS to assess for hydronephrosis). Once identified, such cases require immediate urologic and/or interventional radiology consultation for consideration of emergent decompression, usually by percutaneous nephrostomy.

Guideline-Recommended Antimicrobial Therapy

Tables 5 and **6** shows the recommended empirical antimicrobial regimens for each category of UTI commonly encountered in the ED. The antibiotic choices presented here were derived from the 2011 IDSA UTI treatment guidelines, the Denver Health Antibiotic Guide, and the Sanford Guide.[28,44] We chose these sources because they emphasize using the narrowest spectrum agent and the shortest possible duration. It should be noted that the IDSA guidelines predate widespread emergency of resistance to commonly prescribed oral antibiotics such as TMP/SMX and fluoroquinolones. Importantly, the IDSA guidelines for uncomplicated UTIs are currently under review with new recommendations pending as of this publication. The IDSA also plans to release guidance for complicated UTIs soon as well.

Where possible, however, providers should refer to their hospital-specific empirical therapy guidelines, based on their local hospital antibiogram. In addition, patient-specific risk factors for antibiotic resistance should be taken into consideration, particularly previous isolation of a resistant uropathogen. The review of prior urine culture results should be a routine component of selecting empirical UTI treatment. Complicated patients may require consultation with infectious diseases specialist or infectious disease pharmacist.

Table 5
Empirical antibiotic choices for urinary tract infection in emergency department patients being discharged

Condition	Recommendation
Asymptomatic Patient	Do not treat
Asymptomatic bacteriuria in pregnancy	Cephalexin 500 mg PO QID for 5 days Amoxicillin–clavulanate 875/125 mg PO BID for 5 days Nitrofurantoin 100 mg PO BID for 5 days (after 1st trimester if other options are not available)
Uncomplicated cystitis	Preferred Nitrofurantoin 100 mg PO BID for 5 days *Avoid for CrCl < 30 mL/min* Alternatives Cephalexin 500 mg PO TID for 5 days Fosfomycin 3 g PO once TMP/SMX 1 160/800 mg PO BID for 3 days[a] Amoxicillin/clavulanate 875 mg PO BID for 5 days Cefadroxil 500 mg PO BID for 5 days
Pyelonephritis	Amoxicillin/clavulanic acid 875 mg PO BID for 7 days Cephalexin 1000 mg PO TID for 7 days Levofloxacin 750 mg PO daily for 5 days[b] TMP-SMX 160/800mg PO BID for 7 days[b]
Recurrent UTI	Empirical therapy based on prior cultures and susceptibilities. Obtain urinalysis and culture.

Empirical therapy recommendations based on normal renal function; dose adjustments may be necessary.

[a] If local prevalence of TMP/SMX resistance is less than 20% or confirmed susceptible by urine culture.

[b] If local prevalence of TMP/SMX or fluoroquinolone resistance < 10% or confirmed susceptibile by urine culture.

ANTIMICROBIAL STEWARDSHIP IN THE EMERGENCY DEPARTMENT

Why Stewardship in the Emergency Department Matters

Among patients presenting to the ED, 13% will leave with an antibiotic prescription, with UTIs being one of the most common indications.[45,46] Only 32.7% to 56.6% of these prescriptions are found to be appropriate.[45,47] Inappropriate drug choice, drug dose, or drug duration can all result in deleterious downstream effects, including adverse drug events that require subsequent ED visits or hospitalization.[48] Antimicrobial stewardship (AMS) programs, initially developed for inpatient setting, have begun to expand to the outpatient and ED settings. Recently, Goebel and colleagues published the "Five Ds" for outpatient AMS programs, specifically focused on the management of UTIs[48] see (**Fig. 2**). To increase its relevance to the ED, for the fifth "D," we can replace "de-escalation" with "diagnosis."[49]

Optimizing Empirical Drug Selection for Potential Drug-Resistant Urinary Tract Infections

Increasing rates of resistance to commonly recommended empirical therapy for UTIs present a challenge for ED providers. This is particularly true for complicated UTIs, where the risk of receiving inappropriate empirical therapy is highest. To reduce the risk of inappropriate empirical therapy, ED providers should refer to institution-specific antibiogram data and risk stratification tools wherever possible. These

Table 6
Empirical antibiotic choices for urinary tract infection in emergency department patients being admitted

Condition	Recommendation
Uncomplicated pyelonephritis	Low-risk for multidrug-resistant organism[a]: Ceftriaxone 1 g IV Q24H Confirmed severe PCN allergy: Levofloxacin 500 mg IV/PO Q24H
Complicated pyelonephritis ± gram-negative bacteremia	Cefepime 2 g IV Q12H OR piperacillin/tazobactam 3.375–4.5 g IV Q6H *Review recent urine culture data to guide therapy* High risk for MDRO[a]: Ertapenem 1gm IV q24H OR Meropenem 1 gm IV q8H (concern for *Pseudomonas aeruginosa*) plus vancomycin 15 - 20 mg/kg IV q8h to q 12h *Review recent urine culture data to guide therapy* Severe penicillin allergy: Levofloxacin 750 mg IV/PO Q24H plus gentamicin 3–5 mg/kg IV OR Amikacin 4–7 mg/kg IV Oral step-down therapy: TMP/SMX 160/800 mg Q12H to complete 7 total days OR Levofloxacin 750 mg PO Q24H to complete 5–7 total days OR Ciprofloxacin 500 mg Q12h to complete 5 - 7 days
Complicated UTI/CAUTI	Above, plus remove or exchange catheter

Empirical therapy recommendations based on normal renal function; dose adjustments may be necessary. These regimens represent a potential approach to empircal treatment and should be adjusted based on individual patient considerations and local antibiotic resistance patterns.

[a] Previous infection or colonization with antibiotic resistant gram-negative bacteria, residence in a nursing facility, recent broad-spectrum antibiotics, recent or extensive health care exposure.

typically combine national guideline recommendations, with local microbiology data and local drug acquisition costs. In addition, because resistance profiles differ between urinary and nonurinary gram-negative isolates and between those from inpatients and outpatients, outpatient/ED-specific antibiograms that include only urinary isolates can be developed. These can be used to guide individual empirical therapy and develop locally validated treatment guidelines.[11,50] ED AMS programs that leverage such local antibiograms and site-specific treatment algorithms have been shown to improve prescribing practices and are associated with decreased 30-day return visits.[51]

Caution Using Fluoroquinolones

Fluoroquinolones are no longer first-line agents for uncomplicated cystitis. In the 2011 IDSA uncomplicated UTI guidelines, ciprofloxacin and levofloxacin were noted to be efficacious but associated with a high risk of collateral damage and adverse drug events.[28] The Food and Drug Administration issued a black box warning in 2016 that highlighting the potentially disabling and irreversible side-effects of fluoroquinolones, such as tendon rupture, peripheral neuropathy, and central nervous system effects.[52] As recently as 2010, approximately 40% of uncomplicated UTIs were treated with fluoroquinolones.[53] Rates continued to be high even after issuance of the black box warning.[54–56] Various AMS interventions have decreased unnecessary prescribing of fluoroquinolones in the ED. Combining an uncomplicated UTI order

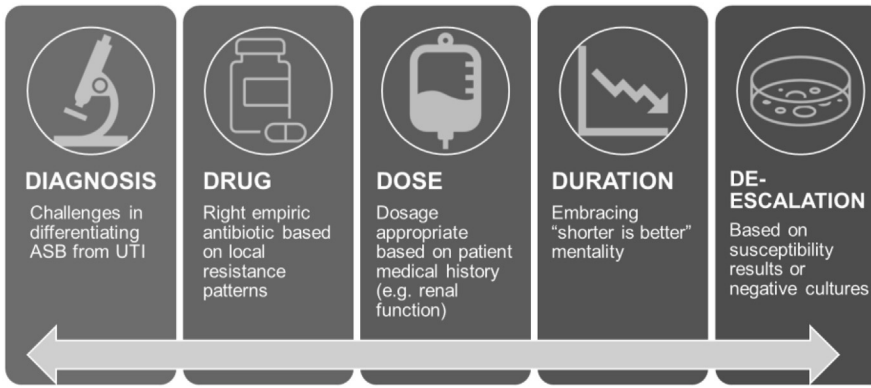
DIAGNOSIS
Challenges in differentiating ASB from UTI
DRUG
Right empiric antibiotic based on local resistance patterns
DOSE
Dosage appropriate based on patient medical history (e.g. renal function)
DURATION
Embracing "shorter is better" mentality
DE-ESCALATION
Based on susceptibility results or negative cultures

Fig. 2. The five "Ds" of stewardship in the emergency department. (*Adapted from* Goebel MC, Trautner BW, Grigoryan L. The Five Ds of Outpatient Antibiotic Stewardship for Urinary Tract Infections. *Clin Microbiol Rev.* 2021 Dec 15;34(4):e0000320.)

set for that de-emphasized fluoroquinolones with an AMS audit and feedback decreased fluoroquinolone prescriptions by 30%.[57] Guidelines, ED-specific urine antibiograms, education, and feedback improve antibiotic prescribing for UTIs and such improvements have been shown to be sustainable with recurrent education and feedback.[58]

Optimizing Drug Dose and Duration

Optimizing antimicrobial therapy for UTIs involves not only choosing the right antibiotic but also choosing the correct dose and duration. When ED patients are prescribed the right antibiotic for the indication, the dose and duration may still differ from what is recommended.[59,60] There is increasing evidence that shorter courses of therapy are associated with similar clinical cure rates compared with traditional longer courses but with lower risk of antimicrobial-related adverse events. Studies have demonstrated the efficacy of short duration therapy for women with uncomplicated cystitis and men with afebrile UTIs.[61,62] For uncomplicated cystitis in women, 5 days of nitrofurantoin, 3 days of TMP/SMX, and single dose of fosfomycin are recommended. For oral beta-lactams, such as cephalexin, the recommended duration is 5 to 7 days. For men with afebrile UTI, 7 days of antibiotics (fluoroquinolone or TMP/SMX) has been proven sufficient. However, an randomized controlled trial (RCT) involving men with febrile UTI was not able to demonstrate noninferiority of a shorter course regimen.[63] The use of indication-based antimicrobial order sets and electronic discharge prescriptions increased optimal agent selection (61% to 80%, $P < .001$), optimal dose selection (67% to 78%, $P = .036$), and optimal duration (26% to 34%, $P = .13$).[64] A multifaceted intervention combining provider education, local treatment protocols, and order sets also demonstrated significant improvements in guideline-concordant antimicrobial selection and duration (41% to 84%, $P < .001$).[65]

Diagnostic Stewardship

Since UTI diagnosis is heavily influenced by test ordering behavior and the tests are plagued by false positives, the so-called diagnostic stewardship, which takes place upstream of treatment decisions, has a high potential to improve diagnosis and thus improve downstream antimicrobial prescribing.[66] Many of the UTI diagnostic stewardship interventions studied in the inpatient setting can also be successfully

applied in the ED.[67] **Table 7** shows the examples of diagnostic stewardship interventions that have been studied in the ED. Interventions aimed at urine culture orders require an interdisciplinary approach involving pharmacy, health IT, and clinical microbiology. Changing the electronic health record end user interface by adding ordering indications and clinical decision support has been shown to improve culturing.[68] Another intervention is conditional reflex urine culturing whereby urine cultures that were ordered are automatically canceled if they do not meet predefined criteria from the UA; this is the opposite practice of reflex urine cultures, which are automatically added based on the UA.[70] Conditional reflex urine culturing has been shown to improve urine culturing rates when implemented as a stand-alone intervention.[70,71,75] Least likely to impact practices in the ED are diagnostic stewardship interventions that change the way urine cultures are reported. These include changing which antimicrobial susceptibilities are reported, modifying and limiting report information, and providing nudges to reduce treatment of ASB.[73,74,76]

Asymptomatic Bacteriuria

Although true UTIs are undeniably common in the ED, the lack of specificity of both symptoms and UA results leads to significant overdiagnosis. Contributing to this overdiagnosis is the common occurrence of leukocytes and bacteria in urine without associated genitourinary symptoms, termed ASB. ASB rarely leads to subsequent infection or negative sequelae.[43,77] In populations with high rates of ASB, including spinal cord injury patients, immune compromised patients, and elderly adults with functional or cognitive impairment, the risk of antibiotic-related adverse events outweighs the potential benefits of clearing the bacteriuria. The challenge presented by ASB is particularly significant in elderly patients presenting for falls or altered mental status, where pyuria and bacteriuria in the absence of fever or genitourinary symptoms is a major driver of inappropriate antibiotic use.[78,79] Such inappropriate antibiotic use occurs across all settings, often beginning in the ED. In a 43-hospital study of adult patients with ASB, 74% received antibiotic therapy, often initiated in the ED.[80] This was associated with prolonged hospitalization and development of *C difficile* infection. Many AMS and diagnostic stewardship initiatives are directed toward deceasing the misdiagnosis of ASB as UTI and preventing unnecessary exposure to antibiotics.

COMMON URINARY TRACT INFECTION-RELATED DILEMMAS IN THE EMERGENCY DEPARTMENT

Altered Mental Status and Falls with Asymptomatic Bacteriuria

Elderly patients with chronic pyuria and bacteriuria often present to the ED with altered mental status, delirium, behavioral change, or after a fall, but without fever or specific symptoms or signs of UTI. In practice, these patients are often treated with antibiotics for a presumed UTI, especially if there is dementia or other conditions that limit the ability to communicate.[81] In response to this challenge, expert bodies like the IDSA have sought to promote a watch-and-wait strategy for admitted patients without classic UTI symptoms, particularly in the context of known chronic ASB or a competing diagnosis that explains the presentation.[42,82] Here is an example of the relevant conversation with the admitting hospitalist: “Mr. Jones is confused with asymptomatic bacteriuria and has no other clinical signs of infection, bacteremia or sepsis. I suspect the confusion is due to a new benzodiazepine prescription and recommend that we pursue a ‘medication holiday’ strategy. I have not started antibiotics, so we can observe and await urine culture results.”

Table 7
Examples of urinary tract infection-related stewardship interventions

Strategy	Description	Challenges
Clinical indications[68]	Must select from list of evidence-based symptoms prior to ordering urine culture	Work-around possible
Clinical decision support[69]	Incorporate evidence-based guidance into EMR to guide urine culture ordering	Time-consuming to implement; need health IT resources
Reflex urine culturing[70–72]	Limit processing or urine cultures based on predefined criteria (ie, WBC on UA)	May still yield positive cultures in patients with ASB
Cascade reporting[73]	Restricting reporting of broad-spectrum antibiotics in favor of more narrow-spectrum agents for cultures growing *E coli* and *Klebsiella* spp.	Extra work for providers when specific susceptibilities needed; can be ignored
Modified reporting[74]	Report minimal results or interpretation of results in the EMR	Can be ignored

Adapted from Goebel MC, Trautner BW, Grigoryan L. The Five Ds of Outpatient Antibiotic Stewardship for Urinary Tract Infections. *Clin Microbiol Rev.* 2021 Dec 15;34(4):e0000320.

Table 8
Less common urinary infections encountered in emergency department practice

Scenario	Common Pitfall	Recommended Approach	Empirical Antibiotics
Chronic cystitis or interstitial cystitis[88]	Chronic bladder pain in the absence of other explanatory etiologies. Common in chronic regional pain syndromes.	UA and culture typically normal. Discharge with referral to urology or uro/gyn. May consider amitriptyline or pelvic floor physical therapy.	Not recommended.
Renal or perinephric abscess[89]	Easily missed diagnosis. Requires IV antibiotics and percutaneous surgical drainage	Obtain a CT scan for patients with pyelonephritis symptoms that are severe or not improving with antibiotics, especially if possibility of obstructing process.	Vancomycin 20–35 mg/kg intravenous loading dose + cefepime 1 g intravenously
Ureterolithiasis with infection[90]	Anchoring on ureterolithiasis diagnosis with checking a urinalysis.	8%–15% of kidney stones have urinary coinfection. Fever, urinary symptoms, or leukocytosis should increase suspicion. Consult urology for potential surgical intervention.	If admitted: ceftriaxone 1 g intravenously If discharged: ciprofloxacin 500 mg orally twice daily for 5–7 d
Urethritis in men[91]	Misinterpreting an STI as a UTI	Question all male dysuria patients about penile drip and sexual habits. Have a low threshold for GC/chlamydia testing.	Ceftriaxone 500 mg IM × 1 (GC) plus azithromycin 1 g PO × 1 (chlamydia)

Cloudy or Foul-Smelling Urine

Cloudy urine often results from precipitated phosphate crystals in alkaline urine, though pyuria also can be the cause. Similarly, a strong odor may be caused by urea in a concentrated specimen rather than a UTI.[83] In general, visual and olfactory inspection of urine, in the absence of UTI symptoms, is not helpful in diagnosing UTI. A study of 100 urine samples from women at a university hospital was tested for the ability to read newsprint through the sample. The sensitivity, specificity, and positive and negative predictive values of legibility, as compared to culture, were 13.3%, 96.5%, 40.0%, and 86.3%, respectively.[84] Here is an example of the relevant conversation with the ED nurse:

Registered nurse (RN): "I collected a urine sample on our patient with a migraine just in case. It looks cloudy. Should I send it for urinalysis?"

ED provider: "The patient does not have urinary symptoms and cloudy urine can be related to hydration status. Let's hold off on send the UA for now."

"Positive" Urine Culture When the Urinalysis Has Greater Than 5 Squamous Epithelial Cells per High-Powered Field

An adequate specimen has fewer than 5 epithelial cells per low-power field on UA. Urine culture results from a contaminated sample are not reliable. Contaminated specimens should be recollected either using true clean-catch methods or by in-and-out catheterization.[85]

Sterile Pyuria

Sterile pyuria refers to white blood cells on the UA without the presence of bacteria. While sterile pyuria sometimes represents a contamination of the urine sample with vaginal leukocytes from vaginal secretions, it can also be a clue to more other unusual or serious illnesses. The differential diagnosis for sterile pyuria includes intra-abdominal infections adjacent to the bladder (eg, appendicitis), sexually transmitted infections, and UTIs from atypical organisms (ie, *Ureaplasma urealyticum*).[86] There is strong evidence that STIs are commonly misdiagnosed as UTIs in women less than 25 year old.[87] The US Center for Disease Control and Prevention recommends that STI testing is obtained routinely along with a UA in this population (**Table 8**).

SUMMARY

Diagnosis and management of UTIs in the ED requires a thoughtful approach, especially given the limited amount and quality of information we are presented with, the potential for severe infection if inadequately treated, and our mandate to provide good antibiotic stewardship. Differentiating cystitis from pyelonephritis from nonurinary pathology is challenging. Emerging antibiotic resistance among uropathogens adds further complexity. Best care entails a careful history and physical examination for urinary signs and symptoms, a nuanced consideration of urine test results and their limitations, and informed judgment as to whether or not to prescribe antibiotics. Once that decision to treat has been made, empirical antibiotic selection should incorporate patient-level factors, national guidelines, and local antibiogram data.

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